PO-0706

Pelvic IMRT with hypofractionated SIB to prostate for high-risk prostate cancer: a phase II study

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Purpose/Objective: Intensity-modulated radiotherapy (IMRT) is being explored in various pelvic malignancies in an effort to mitigate treatment-related toxicity. Moreover, IMRT allows simultaneous differential dose delivery to multiple tumor targets (Simultaneous Integrated Boost, SIB), obviating sequential treatment of an initial volume with a subsequent boost. In addition to the convenience of a shortened treatment duration, theoretical benefits exist for tumor control too, due to hypofractionationed schedule.Our purpose is to evaluate the toxicity of pelvic IMRT with hypofractionated simultaneous integrated boost (SIB) to the prostate for patients with high-risk prostate cancer.
Materials and Methods: A prospective Phase II study was initiated at the end of 2008. The study involved 41 consecutive patients treated definitively with pelvic SIB-IMRT, all of whom also received androgen suppression. The IMRT plans were designed to deliver 67.5 Gy in 25 fractions (2.7 Gy/fraction) to the prostate while simultaneously delivering 56.25 Gy (2.25 Gy/fraction) to the seminal vesicles and 50 Gy (2 Gy/fraction) to the pelvic lymph nodes. All subjects underwent ultrasound-guided transrectal placement of 3 gold intraprostatic fiducial markers. Daily on-line image guidance adjustments were made according to the positions of the fiducial markers.Acute and late genitourinary (GU) and gastrointestinal (GI) toxicities were scored according to the Radiation Therapy Oncology Group (RTOG) grading system.
Results: Fiducial marker placement proceeded without complications. Acute GU toxicity manifested in 12 patients (29%) as grade 1 or 2 urethritis. No patients developed urinary retention and episode of gross hematuria. Acute GI toxicity manifested in 5 patients (12%) as grade 1 or 2. No cases of rectal bleeding were observed. With a follow-up time ranging from 6 to 46 months, no late bladder and rectal complications have been observed so far.
Conclusions: Pelvic IMRT with hypofractionated SIB to prostate was well tolerated in this study, with low rates of Grade 2 acute and late toxicity. SIB-IMRT combines pelvic radiotherapy and hypofractionation to the primary site and offers an accelerated approach to treating high-risk disease. Additional follow-up is necessary to fully define the long-term toxicity after hypofractionated, whole pelvic treatment combined with androgen suppression.

PO-0707

Dosimetric analysis to predict possible GU acute toxicity in prostate cancer treated with volumetric arc therapy

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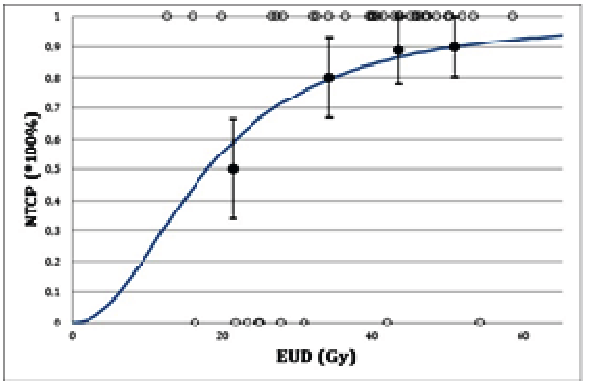
Purpose/Objective: Aim of this study was to test dosimetric parameters able to predict possible acute Genito-Urinary (GU) toxicity in prostate cancer patients treated with Simultaneous Integrated Boost (SIB).
Materials and Methods: A prospective study was performed between January 2011 and March 2012 in our Institution enrolling prostate cancer patients. Radiotherapy was performed with volumetric Arc therapy technique by Linear Accelerator. The Clinical Target Volume, irradiated by SIB-IMRT Technique, included: prostate (CTV1, total dose of 80 Gy) and seminal vesicles (CTV2, total dose of 72 Gy) in forty fractions. We collected a series of CBCT scans during patients' treatment time, and the first five was used for a treatment replanning. For the analysis of the GU toxicity, we divided patients into 2 groups: group A, patients without acute toxicity; group B patients with acute toxicity of any grade. Follow-up was carried out in our Department. Toxicity was graded according to the RTOG criteria. The correlations between acute GU toxicity and bladder dosimetric parameters were tested through logistic models.
Results: 45 patients were included and had a total of 845 CBCT scans. Difference between mean PTV1 (prostate) vs PTV1r was statistically significant (p<0,0001). Difference between mean PTV2 (seminal vesicles) and PTV2r was not statistically significant (p<0,42). Bladder toxicity data were collected in 39/45 (87%) patients. Mean delivered doses of each of the 2 groups were compared: they were significantly higher in group B (group A 23.89 Gy vs group B 42.76 Gy, p=0,02). The area under the curve (AUC) of the mean dose/volume graph, traced for each grade of toxicity, was clear correlated with the grade of toxicity.
For a dose of 25 Gy, the mean dose curve of G0 toxicity was more distant from the other curves G1-2-3: the median V25 was lower for group A (38,89%) against the value of group B (67,87%; p= 0,0085). A V25>50% might express the 80% of probability to envelope bladder toxicity of any grade (AUC =0,793, sensitivity of 73,33 and specificity of 88,89; p=0,0035). A dose-reduction method was used to simplify the evaluation of the toxicity, that is the Equivalent Uniform Dose (EUD). The EUD was significantly higher in patients with GU toxicity (group A 25.10 Gy vs group B 42.13, p=0.02). We built up a DVH-reduction model based on estimated complication probability (NTCP) under EUD of the bladder: patients were distributed on or close to an S slope showing that TCD_{50} was 18 Gy.



Conclusions: IGRT is one method that may reduce toxicity whilst maintaining high delivered treatment doses and personalizing treatment plans. Bladder mean dose and V25 correlate with acute GU toxicity and could better optimize planning procedures in treatment validation. Further studies with bigger series are still needed to confirm these finding.

PO-0708

Reliability and ideal cut-off of PSADT in patients candidate to early salvage radiotherapy after prostatectomy.

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Purpose/Objective: PSA doubling time (PSADT) has a recognized role in patients (pts) candidates to salvage radiotherapy (SRT) for a biochemical recurrence (BR) after radical prostatectomy (RP). Its role and the most widely accepted cut-off (10-12 months) discriminating between more likely local relapse and systemic progression were retrospectively addressed in pts typically undergoing SRT with PSA values at SRT much greater than those currently suggested. The study was aimed at investigating its reliability and ideal cut-off in pts candidates to very timely SRT.
Materials and Methods: The study included 200 node-negative pts who received SRT for BR after RP between 1994 and 2010. BR was defined as the first of two or more consecutive and increasing PSA values >0.20 ng/mL after RP. PSADT was computed based on an increasing set of hormono-naïve PSA values starting from the first value ≥0.10 ng/mL up to the beginning of SRT (overall PSADT). PSADT was also computed at 3, 6, 9, 12, 18, 24 months from the first observation ≥0.10 ng/mL, or on 2, 3, 4, 5, 6 consequent measurements, when available. Biochemical relapse-free survival (bRFS) after SRT was considered as primary endpoint and was set as the time from the beginning of SRT to PSA failure after SRT (i.e. a single PSA >0.20 ng/mL after an SRT-induced nadir or an increase of serum PSA despite SRT).
Results: After a median follow-up of 80.8 months, 44 pts (22%) experienced a PSA failure after SRT (33 within 5-years). The median overall PSADT was 8.18 months, based on a median of 4 PSA observations. Cox regression analysis selected as significant predictors for bRFS: Gleason score (2-6 vs 7-10), PSA at SRT, dose of RT, overall PSADT and time from RP to the first post-RP PSA value ≥0.10 ng/mL.

Notably, the time from RP to BR was not significant. The probability of 5-yr bRFS was significantly predicted by overall PSADT (p<0.0001, by logistic regression), with the optimal cut-off set at 5.79 months (sensitivity=0.67, specificity=0.72) by ROC analysis.The PSADTs, computed at different time points or with a different number of observations were always significantly correlated to the overall PSADT, (Spearman's correlation). However, only the PSADTs computed at ≥9 months or based on ≥4 observations emerged as significant predictors of 5-yr bRFS (logistic regression) with most informative cut-offs of 4.6 and 6.58 months, respectively. Finally, the median PSADT increased as a function of time and number of observations, thus suggesting an effect of the dynamic selection of the patients (apparently, those with the poorer prognosis had started SRT earlier).
Conclusions: Only PSADT calculated ≥9 months after the first value ≥0.10 ng/mL and/or on ≥4 observations resulted to be predictive of the risk of treatment failure following SRT. This may limit its role in selecting patients to be addressed to very early SRT. Of note, our optimal cut-offs ranged from 4.6 to 6.58 months.

PO-0709
Acute toxicity in post-operative prostate cancer: hypofractionation-vmat versus conventional-3DCRT.
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Purpose/Objective: To retrospectively evaluate and compare the incidence of acute genito-urinary (GU), upper gastrointestinal (uGI) and rectal (lGI) injuries of hypofractionation by volumetric modulation arc therapy or VMAT (Hypo-RapidArc group) and conventional fractionation by three dimensional conformal radiotherapy (3DCRT group) in patients with localized prostate cancer treated with prostatic bed irradiation, after radical prostatectomy.
Materials and Methods: Between 2007 and 2012, 84 consecutive patients with clinically localized prostate cancer patients submitted to radical prostatectomy were irradiated to prostate bed: 41 with 3DCRT and 43 with VMAT by RapidArc. The median age was 67 and 68,5 years for 3DCRT and Hypo-RapidArc group respectively. The median dose to the prostatic bed was 70 Gy (70 - 76) with 2 Gy per fraction in 3DCRT group and 70Gy (70 – 72,4) with 2.5Gy (2.5 – 2.55) per fraction in the Hypo-RapidArc group. After radical prostatectomy, the median time to RT was 15 and 16 months respectively in 3DCRT and Hypo-RapidArc group. Acute GU, uGI e lGI toxicities after radiation treatment were evaluated using RTOG/EORTC medical scoring system.
Results: Acute G2 GU toxicities were better in Hypo-RapidArc group compared to 3DRCT group: 12% versus 17% respectively in the two groups. Inversely, for Acute G2 intestinal toxicities, 3DCRT was well tolerated: for uGI no G2 were found in 3DCRT versus 7% in Hypo-RapidArc group; for lGI G2 toxicities7% in 3DCRT versus 18% in Hypo-RapidArcgroup. No G3 or greater toxicities were found in both groups. In both groups the PTV coverage is suitable: PTV mean dose is 99.4±1.0% and 99.8±0.9% and $V_{95\%}$ 96.3±3.6% and 95.7±8.9 for 3DRCT and RA group respectively. For 3DRTC group the Rectum received a mean dose of42.1±9.4 Gy (with V_{65Gy} equal to 26.9±10.0 %) and the Bladder received 69.3±17.2Gy in mean (with the V_{65Gy} equal to 45.0±19.5%); and for RA group the dose decreased to 37.2±5.2 Gy (V_{65Gy} 9.6±5.1%) and 39.2±13.4 (V_{65Gy}25.2±14.4%) for Rectum and Bladder.
Conclusions: The results of our study of 84 patients have shown that acute G2 GU are reduced using hypofractionation by RapidArc compared to conventional fractionation by 3DCRT, while acute G2 GI toxicities remains significantly better for the last one. Remarkable is the absence of G3 using hypofractionation by RapidArc as well as recorded previously with conventional fractionation by 3DCRT. Longer term data are awaited for late toxicity profiles and clinical efficacy in Hypo-RapidArc group of patients.

PO-0710
The necessity and effectiveness of adaptive replanning of patients having large prostate rotations
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Purpose/Objective: To asses the effectiveness of online monitoring of prostate rotation as an indicator of the need for adaptive replanning in prostate patients treated with IMRT; to evaluate the possibility to predict large interfraction prostate rotations based on rectal filling on the planning CT.

Materials and Methods: From a population of 640 prostate cancer patients treated with IMRT combined with online marker-based setup correction, 26 patients who exhibited frequent and large (>10 °) prostate rotations were selected for a repeat CT scan and adaptive replanning. The effectiveness of adaptive replanning of these patients was assessed by evaluating the relative decrease in the frequency of large prostate rotations. The correlation between rectal filling as determined on the planning CT and the frequency of large prostate rotations was analyzed. Also, for these 26 re-planned patients the second planning CT scan was imported in the initial IMRT plan and the target coverage was evaluated in order to assess the potential impact of no action on this group of patients.
Results: For the 26 patients that were re-planned, the frequency of large prostate rotations significantly decreased by 80.7% on average (p<0.001) during the fractions treated with the adapted plan. No significant correlation was found between the rectum volume, cross-section or diameter on the planning CT and the frequency of prostate rotations (p>0.05), however there seems to be a higher risk of large rotations in patients with a rectum diameter larger than 5 cm at the level of the prostate base (p=0.03). If these patients had not been re-planned, due to the systematic change in prostate orientation the PTV coverage would have decreased to 90.2% on average, although the CTV would remain adequately covered for all patients.
Conclusions: For prostate cancer patients treated with IMRT combined with fiducial-based online position verification, a relatively simple prostate rotation monitoring protocol is sufficient to select the patients in need of adaptive replanning. Rectal filling on the planning CT scan is not a significant predictor of the frequency of large prostate rotations, although patients with a large diameter of the rectum on the planning CT seem to have a higher chance of having large prostate rotations.

PO-0711
Radical radiotherapy for prostate cancer in octogenarians: A single centre experience
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Purpose/Objective: As male life expectancy increases throughout the developed world the incidence of prostate cancer is also increasing. Better diagnostics and raised public awareness has also contributed to this. A significant survival benefit favouring hormone therapy and radical radiotherapy over hormone therapy alone in locally advanced prostate cancer has been shown in recent studies. Radical radiotherapy technology for prostate cancer has evolved significantly aiming to reduce toxicity to normal tissues. Taking 10 year survival as the standard for assessing the use of radical treatment, we looked at the outcomes of patients who received radical radiotherapy for prostate cancer commencing after their 80th birthday.
Materials and Methods: Data was collected retrospectively of all patients treated with radical radiotherapy for prostate cancer after their 80th birthday at our centre. From 2001 to 2012 a total of 25 patients were suitable for inclusion. Complete data was available for 20 patients. Key measures were patient's prostate cancer risk category, predicted 10 year survival (based on Charlson comorbidity index) and actual disease free survival.
Results: The mean age of patients was 80.76 years (range: 80 to 84). Patients received external beam radiotherapy as per local guidelines at a dose of 74 Gray in 37 fractions (80% of cases). Patients treated earlier received treatment doses ranging from 64 Gray in 32 fractions to 70 Gray in 30 fractions. 84% of patients had stage T3 disease, PSA≥ 20ng/ml or Gleason score of ≥ 8 making them high risk according to National Institute for Clinical Excellence (NICE) criteria. The remaining patients were categorised as intermediate risk. No patients had nodal or distant metastases on imaging. All patients had a predicted 10 year survival of ≤ 2.25%, based on the Charlson comorbidity index. It is known that 4 patients have died. In 2 cases, the cause of death was unrelated; one from primary lung cancer and one from oesophageal cancer. The median disease free survival was 24 months (range: 4 to 104). Median follow-up was 22 months.
Conclusions: Patients in this age group have a low 10 year survival even without the presence of prostate cancer. By including intermediate to high risk prostate cancer, as in this series, this becomes even less. However, this 12 year series demonstrates that with careful selection a reasonable disease free survival can be achieved in this group of elderly men. Rather than basing decisions on predicted 10 year survival, radical radiotherapy should be carefully discussed with men over 80 with potentially curable prostate cancer on a patient by patient basis. We intend to create a prospective database of such patients in the future to further investigate the